REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and remarks presented herewith, which place the application into condition for allowance, or in better condition for appeal.

Status of the Claims and Formal Matters

Claims 1-4, 13, 18-24, 26, and 27 are currently pending in this application. In order to advance prosecution, claims 1, 19,24 and 26 have been amended. Amendments to the claims find support at page 3, lines 21-22, page 5, lines 5-6 and, in particular, page 4, lines 24-26 and Example 5. Applicants reserve the right to claim withdrawn and/or cancelled subject matter in co-pending applications.

Rejections under 35 U.S.C. §103(a)

Claims 1-4, 13, 18-24, 26 and 27 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin et al, (U.S. 6, 610, 839), "Morin" in view of Chin et al., (U.S. 6,197,599), "Chin". In view of amendments to claim 1 and remarks presented herewith, Applicants request reconsideration and withdrawal of the rejection.

The methods of the instant invention allow for specific modification, in one pot, of every member of a cDNA library in a manner which does not rely on any knowledge of the sequence of individual genes. This allows one of ordinary skill in the art to tag a library of DNA sequences and subsequently purify and immobilize the tagged expression products in a single step, via the marker tag to a solid support in a spatially defined format.

Morin relates to binding of a tagged polypeptide to a molecule immobilized on a solid support such as a resin. However, purification and immobilization as described by Morin is not to a single support but to variety of supports within the same resin. There is no attempt to purify such polypeptides in a spatially defined manner on one single support, as described in the instant application.

Morin does not teach or suggest the method of generating a protein array from a library of two or more non-identical target DNA sequences comprising (a) inserting a marker DNA sequence in frame immediately following a start codon of each of target DNA sequences or immediately preceding a stop codon of each of the target DNA sequences or both, to form library of modified DNA sequences which encode a library of modified amino acid sequences each comprising a marker moiety; (b) expressing the library of modified target amino acid sequences from the library of modified DNA sequences; (c) purifying and immobilizing each of the modified target amino acid sequences to a solid support in a single step, wherein the marker moiety of the target modified amino acid sequences is directly attached to the solid support in a spatially defined format, thereby generating a protein array, and (d) washing said solid support to remove unbound proteins.

Chin does not remedy the deficiencies of Morin. Chin relates to construction of an array of biomolecules on a single solid support which requires that each individual member of the array be purified and immobilized separately. Chin does not teach or suggest the method of generating a protein array from a library of two or more non-identical target DNA sequences comprising (a) inserting a marker DNA sequence in frame immediately following a start codon of each of target DNA sequences or immediately preceding a stop codon of each of the target DNA sequences or both, to form library of modified DNA sequences which encode a library of modified amino acid sequences each comprising a marker moiety; (b) expressing the library of modified target amino acid sequences from the library of modified DNA sequences; (c) purifying and immobilizing each of the modified target amino acid sequences to a solid support in a single step, wherein the marker moiety of the target modified amino acid sequences is directly attached to the solid support in a spatially defined format, thereby generating a protein array, and (d) washing said solid support to remove unbound proteins.

Applicants respectfully submit that instant claims are not obvious over Morin in view of Chin. Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, office personnel must explain why the

difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art.[1] This explanation is clearly lacking with respect to the presently claimed invention

As stated by the Supreme Court, the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham* v. *John Deere Co.*[2/] The factual inquiries enunciated by the Court are as follows:

(1) Determining the scope and content of the prior art;
(2) Ascertaining the differences between the claimed invention and the prior art; and
(3) Resolving the level of ordinary skill in the pertinent art.3

As is explained by the Federal Circuit, the motivation to combine is part of the discussion in determining the scope and content of the prior art,[4/] and where all claim limitations are found in a number of references, the fact finder must determine "[w]hat the prior art teaches... and whether it motivates a combination of teachings from different references."[5/] While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ('TSM') test in an obviousness inquiry, the Court acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination. Moreover, the [Supreme] Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the Graham analysis."[6/]

---

[1] MPEP § 2141

[2/] 383 U.S. 1, 148 USPQ 459 (1966); reaffirmed and relied upon in KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 82 USPQ2d 1385 (2006).

[3/] *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966); reaffirmed and relied upon in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385 (2006).

[4/] *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006); *citing SIBIA Neurosciences, Inc. v. Cadus Pharma. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000).

[5/] *Id.* citing *In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004).

[6/] *Takeda*, 492 F.3d at 1356-1357, quoting KSR, 127 S.Ct. at 1731.

Using the above as guidance, Applicants assert that one of ordinary skill in the art would not have had motivation to modify the teachings of Morin in view of Chin to arrive at the claimed invention.

Accordingly, since Morin in view of Chin fails to teach or suggest every element of the claims, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. 103(a).

Claim 17 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin in view of Chin, and further in view of Ben-Bassat (U.S. 4,865,974), "Ben-Bassat". In view of the previous cancellation of claim 17, the rejection under 35 U.S.C. §103(a) is now moot. Applicants request withdrawal of the rejection.

Claim 24 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin in view of Chin and further in view of Orr et al., (US. 5,741,645), "Orr" and Nielsen et al., (U.S.6,350,853), "Nielson". In view amendments to independent claim 1 and remarks presented herewith, Applicants request reconsideration and withdrawal of the rejections.

As provided above, Applicants respectfully disagree with the rejection under §103(a), because the teachings of Morin in combination with Chin do not result in the present invention as claimed. Morin and Chin, considered alone or in combination, do not describe a method of making a protein array by tagging a library of two or more target DNA sequences, and subsequently purifying and immobilizing the tagged expression products directly to a single solid support via the tag moiety, in a single step and in a spatially defined format.

Orr does not cure the deficiencies of Morin and Chin. Orr relates to an isolated 1.2 Mb region of human chromosome 6 that contains a highly polymorphic CAG repeat region and which correlates to the spinocerebellar ataxia type 1 locus (SCA1). Further, Orr discloses the presence of naturally-occurring dinucleotide repeats that are present on either side of a large 1.2 Mb stretch of chromosome 6 allows one of skill in the art to identify approximately where SCA1 locus is located. These naturally-occurring well known dinucleotide repeats are present in the chromosome and are not inserted. Orr does not provide a method for inserting sequences in-

frame at a specific location in a sequence-independent manner, such as without prior knowledge of the sequence to be modified.

Orr does not teach or suggest the method of generating a protein array from a library of two or more non-identical target DNA sequences comprising (a) inserting a marker DNA sequence in frame immediately following a start codon of each of target DNA sequences or immediately preceding a stop codon of each of the target DNA sequences or both, to form library of modified DNA sequences which encode a library of modified amino acid sequences each comprising a marker moiety; (b) expressing the library of modified target amino acid sequences from the library of modified DNA sequences; (c) purifying and immobilizing each of the modified target amino acid sequences to a solid support in a single step, wherein the marker moiety of the target modified amino acid sequences is directly attached to the solid support in a spatially defined format, thereby generating a protein array, and (d) washing said solid support to remove unbound proteins.

Nielsen does not cure the deficiencies of Morin and Chin. Nielsen merely relates to peptide nucleic acids (PNA) having a polyamide backbone which are conjugated to lipophilic groups and are incorporated into liposomes. Nielsen does not teach or suggest the method of generating a protein array from a library of two or more non-identical target DNA sequences comprising (a) inserting a marker DNA sequence in frame immediately following a start codon of each of target DNA sequences or immediately preceding a stop codon of each of the target DNA sequences or both, to form library of modified DNA sequences which encode a library of modified amino acid sequences each comprising a marker moiety; (b) expressing the library of modified target amino acid sequences from the library of modified DNA sequences; (c) purifying and immobilizing each of the modified target amino acid sequences to a solid support in a single step, wherein the marker moiety of the target modified amino acid sequences is directly attached to the solid support in a spatially defined format, thereby generating a protein array, and (d) washing said solid support to remove unbound proteins.

Applicants respectfully submit that instant claims are not obvious over Morin in view of Chin in view of Orr and in view of Nielsen. Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art.[7] This explanation is clearly lacking with respect to the presently claimed invention

CONCLUSION

Favorable action on the merits is respectfully requested. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

Applicants believe no additional fees are due with the filing of this Amendment and Response; however, if any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number: **50-0311**, Customer Number: **35437**, Reference Number: **27353-501 UTIL.**

Respectfully submitted,

Dated: October 7, 2008

Ivor R. Elrifi, Reg. No. 39,529
Johnson, David, Reg. No. 41,874
Ilona Gont, Reg. No. 58,714
Attorneys/Agent for Applicants
c/o MINTZ, LEVIN, *et al.*
666 Third Avenue-24th Floor
New York, New York 10017
Telephone: (212) 935-3000
Telefax: (212) 983-3115

[7] MPEP § 2141